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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,668	05/06/1999	JONATHAN M. GERSHONI	27/135	1117

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	16

DATE MAILED: 02/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/297,668	GERSHONI ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *144-176* is/are pending in the application.

4a) Of the above claim(s) *157-158 and 171-176* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *144-156 and 159-170* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I in Paper No. 15, claims 144-156 and 159-170, is acknowledged. The traversal is on the grounds(s) that the Application is the national phase of a PCT but the examiner's reasons for restriction are based on U.S. rules and not the PCT rules. Applicant's arguments are found persuasive. The previous restriction requirement is withdrawn in view of Applicant's arguments and in view of the restriction requirement in accordance with 37 C.F.R. 1.499 as detailed below.

Restrictions

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 144-156 and 159-170, drawn to a method of identifying and producing a peptide.

Group II, claim 157, drawn to drawn to a method of vaccinating.

Group III, claim 158, drawn to a library of peptides.

Group IV, claim 171-175, drawn to a method of identifying and producing an oligonucleotide.

Group V, claim 176, drawn to a library of oligonucleotides.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups I-V appears to be that they all relate to a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological

unit where in the peptide is produced by providing and randomly ligating a plurality of DNA fragments which encode the single biological unit.

However, Marks et al (The Journal of Biological Chemistry, 1992, 267(23): 16007-16010) teach the peptide and method of making the peptide as claimed.

Therefore, the technical feature linking Groups I-V does not constitute a special technical feature as defined by PCT Rule 13.2 because it does not define a contribution over the prior art.

The special technical feature of Group I is considered to be a method of identifying and producing a peptide.

The special technical feature of Group II is considered to be a method of vaccinating.

The special technical feature of Group III is considered to be a library of peptides.

The special technical feature of Group IV is considered to be a method of identifying and producing an oligonucleotide.

The special technical feature of Group V is considered to be a library of oligonucleotides.

Accordingly, Groups I-V are not so linked by the same or a corresponding special technical feature so as to form a single general inventive concept.

3. During a telephone conversation with Mr. Allen Yun on 7 February 2002 a provisional election was made with traverse to prosecute the invention of Group I, claims 144-156 and 159-170. Affirmation of this election must be made by applicant in replying to this Office action. Claims 157, 158 and 171-176 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 144-156 and 159-170 are under prosecution.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 159-171 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 159-171 are indefinite in Claim 159 because the claim is drawn to a method of preparing a library of peptides, but the method does not recite step of library preparation. It is suggested that Claim 159 be amended to recite methods steps of preparing a library e.g. at the end of Claim 159, insert "thereby preparing a library of peptides.".

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 144-146, 149-151, 155, 156, 159-161, 163-165, 169 and 170 are rejected under 35 U.S.C. 102(b) as being anticipated by Huse et al (Science, 1989, 246: 1275-1281).

Regarding Claim 144, Huse et al disclose a method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left

column, first full paragraph). The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein "a single biological unit" is not clearly defined. Given the broadest reasonable interpretation of the claim, the claimed single biological unit encompasses the antibody of Huse et al. Therefore, Huse et al disclose the method as claimed.

Regarding Claim 145, Huse et al disclose the method wherein step (a) comprises cutting said DNA sequence to form said plurality of DNA fragments (page 1278, left column, first full paragraph).

Regarding Claim 146, Huse et al disclose the method wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph).

Regarding Claim 149, Huse et al disclose the method wherein step (b) comprises randomly ligating said plurality of DNA fragments to form at least one ligated fragment and at least partially digesting the ligated fragment to form said library i.e. the light chain fragments and heavy chain fragments are each randomly ligated into vectors and then digested (page 1277, right column, last three lines-page 1278, first three lines).

Regarding Claim 150, Huse et al disclose the method wherein said expression system comprises a plurality of bacteria and step (c) comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph).

Regarding Claim 151, Huse et al disclose the method wherein said expression system comprises a plurality of phage and step (c) comprises inserting one of said library into each of said plurality of phage (page 1278, left column, first full paragraph).

Regarding Claim 155, Huse et al disclose the method wherein the single biological unit is a protein i.e. the single biological unit is an antibody and the fragments provided in (a) are fragments of the antibody (Abstract). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein "a single biological unit" is not clearly defined. Given the broadest reasonable interpretation of the claim, the claimed single biological unit encompasses the antibody of Huse et al. Therefore, Huse et al disclose the method as claimed.

Regarding Claim 156, Huse et al disclose the method wherein the single biological unit is two or more proteins which interact to form a complex i.e. the single biological unit is a light chain and a heavy chain and the light and heavy chain interact to form an antibody complex (Abstract). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein "a single biological unit" is not clearly defined. Given the broadest reasonable interpretation of the claim, the claimed single biological unit comprising two or more proteins encompasses the light chain and heavy chain of Huse et al. Therefore, Huse et al disclose the method as claimed.

Regarding Claim 159, Huse et al disclose a method of preparing a library of peptides comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein "a single biological unit" is not clearly defined. Given

the broadest reasonable interpretation of the claim, a single biological unit encompasses the antibody of Huse et al. Therefore, Huse et al disclose the method as claimed.

Regarding Claim 160, Huse et al disclose the method wherein step (a) comprises cutting said DNA sequence to form said plurality of DNA fragments (page 1278, left column, first full paragraph).

Regarding Claim 161, Huse et al disclose the method wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph).

Regarding Claim 163, Huse et al disclose the method wherein step (b) comprises randomly ligating said plurality of DNA fragments to form at least one ligated fragment and at least partially digesting the ligated fragment to form said library i.e. the light chain fragments and heavy chain fragments were each randomly ligated into vectors and then digested (page 1277, right column, last three lines-page 1278, first three lines).

Regarding Claim 164, Huse et al disclose the method wherein said expression system comprises a plurality of bacteria and step (c) comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph).

Regarding Claim 165, Huse et al disclose the method wherein said expression system comprises a plurality of phage and step (c) comprises inserting one of said library into each of said plurality of phage (page 1278, left column, first full paragraph).

Regarding Claim 169, Huse et al disclose the method wherein the single biological unit is a protein i.e. the single biological unit is an antibody and the fragments provide in (a) are fragments of the antibody (Abstract). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein "a single biological unit" is not clearly defined. Given the broadest reasonable interpretation, the claimed single biological unit encompasses the antibody of Huse et al. Therefore, Huse et al disclose the method as claimed.

Regarding Claim 170, Huse et al disclose the method wherein the single biological unit is two or more proteins which interact to form a complex i.e. the single biological unit is f a light chain and a heavy chain which interact to from an antibody complex (Abstract). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein "a single biological unit" is not clearly defined. Given the broadest reasonable interpretation, the claimed single biological unit encompasses the light chain and heavy chain proteins of Huse et al. Therefore, Huse et al disclose the method as claimed.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 147, 148, 154, 162 and 168 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huse et al (Science, 1989, 246: 1275-1281) in view of Stemmer et al (U.S. Patent No. 5,811,238, filed 30 November 1995).

Regarding Claim 147, Huse et al teach a method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the

identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph) wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph) but they do note teach the cutting is accomplished by mechanically cutting. However, mechanical cutting of DNA was well know in the art at the time the claimed invention was made as taught by Stemmer et al. who teach a similar method of identifying and producing a peptide. Specifically, Stemmer et al teach the similar method comprising providing a plurality of DNA fragments which appear in a DNA sequence encoding a single biological unit (i.e. antibody); creating a library of oligonucleotides by randomly rearranging said fragments (i.e. shuffling); inserting the oligonucleotides into an expression system; expressing and screening the expressed peptide (Column 5, lines 23-50) wherein the fragments are provided by mechanically cutting (Column 17, lines 30-35). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the enzyme digestion of Huse et al with the mechanical shearing as taught by Stemmer et al to thereby eliminate the time and labor involved with DNA digestion and DNA purification following digestion for the obvious benefit of economy of time and labor.

Regarding Claim 148, Huse et al teach the method wherein said fragments are provide by cutting i.e. restriction digestion (page 1278, left column, first full paragraph) but they do not teach the fragments are provided by synthesis. However, synthesis of DNA fragments was well know in the art at the time the claimed invention was made as taught by Stemmer et al. who teach a similar method of identifying and producing a peptide. Specifically, Stemmer et al teach a similar method comprising providing a plurality of DNA fragments which appear in a DNA sequence encoding a single biological unit (i.e. antibody); creating a library of oligonucleotides by randomly rearranging said fragments (i.e. shuffling); inserting the oligonucleotides into an expression system; expressing and screening the expressed peptide (Column 5, lines 23-50) wherein the fragments are synthesized (Column 17, lines 48-52). It would have been obvious to one of ordinary skill in the art at the time the claimed invention

was made to modify the enzyme digestion of Huse et al with the synthesis as taught by Stemmer et al to thereby provide fragments of known sequence and for the obvious benefit of screening known fragments for binding activity. For example, a protein having a known sequence interacts with a ligand, but the fragment of protein which interacts with the ligand is unknown. The skilled artisan would have been motivated to analyze the encoding sequence to identify fragments encoding potential binding activity and to synthesize only those specific fragments and to randomly ligate the fragments to thereby identify and produce discontinuous peptides with bind to the ligand of interest.

Regarding Claim 154, Huse et al teach the method wherein said expression system comprises a plurality of bacteria and step (c) of inserting comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph) but they do not teach the expression system is eukaryotic. However, eukaryotic expression systems were well known in the art at the time the claimed invention was made as taught by Stemmer et al who teach the similar method wherein the expression system is eukaryotic (Column 38, lines 1-42). Additionally, they teach that eukaryotic systems are preferred because the peptide produced in secreted as an intact product (Column 38, lines 5-10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phage expression system of Huse et al with the eukaryotic expression system as taught by Stemmer et al and to insert the library of oligonucleotides into eukaryotic vectors for expression in a eukaryotic cell to thereby express and secret intact peptides as preferred by Stemmer et al for the obvious benefit of obtaining an intact peptide which is secreted and therefore easily purified as taught by Stemmer et al (Column 38, lines 5-10).

Regarding Claim 162, Huse et al teach a method preparing a peptide library comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression

system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph) wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph) but they do note teach the cutting is accomplished by mechanically cutting. However, mechanical cutting of DNA was well know in the art at the time the claimed invention was made as taught by Stemmer et al. who teach a similar method of identifying and producing a peptide. Specifically, Stemmer et al teach the similar method comprising providing a plurality of DNA fragments which appear in a DNA sequence encoding a single biological unit (i.e. antibody); creating a library of oligonucleotides by randomly rearranging said fragments (i.e. shuffling); inserting the oligonucleotides into an expression system; expressing and screening the expressed peptide (Column 5, lines 23-50) wherein the fragments are provided by mechanically cutting (Column 17, lines 30-35). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the enzyme digestion of Huse et al with the mechanical shearing as taught by Stemmer et al to thereby eliminate the time and labor involved with DNA digestion and DNA purification following digestion for the obvious benefit of economy of time and labor.

Regarding Claim 168, Huse et al teach the method wherein said expression system comprises a plurality of bacteria and step (c) of inserting comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph) but they do not teach the expression system is eukaryotic. However, eukaryotic expression systems were well known in the art at the time the claimed invention was made as taught by Stemmer et al who teach the similar method wherein the expression system is eukaryotic (Column 38, lines 1-42). Additionally, they teach that eukaryotic systems are preferred because the peptide produced in secreted as an intact product (Column 38, lines 5-10). It would have been obvious

to one of ordinary skill in the art at the time the claimed invention was made to modify the phage expression system of Huse et al with the eukaryotic expression system as taught by Stemmer et al and to insert the library of oligonucleotides into eukaryotic vectors for expression in a eukaryotic cell to thereby express and secret intact peptides as preferred by Stemmer et al for the obvious benefit of obtaining an intact peptide which is secreted and therefore easily purified, as taught by Stemmer et al (Column 38, lines 5-10).

10. Claims 152, 153, 166 and 167 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huse et al (Science, 1989, 246: 1275-1281) in view of Marks et al (The Journal of Biological Chemistry, 1992, 267(23): 16007-16010).

Regarding Claims 152 and 153, Huse et al teach a method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph) but they do note teach the oligonucleotides are cloned into phage genes coding for a coat protein. Marks et al teach a similar method comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. antibody);

creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 16008, Fig 1 and 2) wherein the said oligonucleotides are inserted into phage genes coding for a coat protein and wherein said coat protein is pIII or pVIII (page 16008, Fig. 2). Additionally, Marks et al teach that by inserting the oligonucleotide in to the coat proteins (e.g. pIII or pVIII) multiple antibodies are displayed on each phage providing higher binding avidity thereby maintaining antibody-antigen binding during washing even for the lower-affinity binding reactions (page 16009, left column, first paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phage in the method of Huse et al by inserting the oligonucleotide in to either the pIII or pVIII coat protein of filamentous phage as taught by Marks et al to thereby express multiple antibodies on each phage and increase binding avidity thereby maintaining antibody-antigen binding during washing and selection steps for the expected benefit of obtaining even lower-affinity binding reactions as taught by Marks et al (page 16009, left column, first paragraph).

Regarding Claims 166 and 167, Huse et al teach a method preparing a peptide library comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph) but they do not

teach the oligonucleotides are cloned into phage genes coding for a coat protein. Marks et al teach a similar method comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 16008, Fig 1 and 2) wherein the said oligonucleotides are inserted into phage genes coding for a coat protein and wherein said coat protein is pIII or pVIII (page 16008, Fig. 2). Additionally, Marks et al teach that by inserting the oligonucleotide in to the coat proteins (e.g. pIII or pVIII) multiple antibodies are displayed on each phage providing higher binding avidity thereby maintaining antibody-antigen binding during washing even for the lower-affinity binding reactions (page 16009, left column, first paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phage in the method of Huse et al by inserting the oligonucleotide in to either the pIII or pVIII coat protein of filamentous phage as taught by Marks et al to thereby express multiple antibodies on each phage and increase binding avidity thereby maintaining antibody-antigen binding during washing and selection steps for the expected benefit of obtaining even low-affinity binding reactions as taught by Marks et al (page 16009, left column, first paragraph) and thereby produce a more complete library as desired.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
February 14, 2002